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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,186	10/09/2001	David Reginald Adams	040283-0192	7541

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EXAMINER
BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/890,186	ADAMS ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE f this communication appears n th cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9-18,29 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-18 and 29* is/are rejected.

7)☒ Claim(s) *11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/24/2003 has been entered.

Applicants' response which included amendment claims 1-4, 9-18, 29, and cancellation of claims 5-8, 19-28 and 30-33,filed on 6/24/2003, is also made of record.

Claims 1-4, 9-18, 29 and 34 are now pending.

In view of applicants' response, particularly amendment to claims 1-4, 9-18 to limit them to pharmaceutical composition, the following apply:

Claim Objections

Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 which dependent on claim 1 recites a trifluoromethyl group as substituents on the aryl ring which outside the scope of claim 1. Note claim 1 is limited to alkyl and cannot include haloalkyl.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 14,16, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mokrosz et al., Med. Chem. Res. 3: 240-248,1993 for reasons of record. To repeat:

Mokrosz et al. teaches rigid arylpiperazines as CNS agents, which include a compound with ethyl group on the piperazine ring. See compound 7 on page 241, and process of making on page 247.

While said compound doesn't anticipate the scope of instant claims in view of the proviso in claim 1, they are very closely related, having a methyl group on the phenyl ring vs. unsubstituted phenyl ring compound of the reference. However, compounds

that differ only in having H vs Me are not deemed patentably distinct absent evidence of superior or unexpected properties. See for compounds that differ only as H vs Me in the phenyl ring, In re Wood 199 USPQ 137; In re Lohr 137 USPQ 548. Thus it would have been obvious to one skilled in the art at the time of the invention was made to expect instant compounds to possess the utility taught by the applied art in view of the close structural similarity outlined above.

Applicants' argument to overcome this rejection by showing comparative example is not persuasive.

The issue is would one trained in the art be motivated make based on the unsubstituted arylpiperazine taught by Mokrosz et al., to make arylpiperazines with a methyl group in the aryl ring, more specifically the N-ethyl-piperazine compound, the closest prior art compound. The rejection is based on this fact and it would be obvious for one trained in the art make such compounds, as he would expect these compounds to possess the utility taught by Mokrosz et al.

Applicants have shown comparative results with the unsubstituted piperazine compound, compound 6 of the prior art over the instant compounds but have not provided any evidence that the instant invention as a class would have unexpected/superior property.

Additionally, applicants should note that the prior art N-ethyl piperazine as shown by Mokrosz et al. is active at the 5HT receptor and hence one would be motivated to make and evaluate the compound with a methyl group in the phenyl ring.

See Ex parte Gelles 22 USPQ 2nd 1318. Note Gelles, especially the following quote: " The evidence relied upon also should be reasonably commensurate in scope with the subject matter claimed and illustrate the claimed subject matter " as a class" relative to prior art subject matter."

Hence the rejection is proper and is maintained.

Claims 1-4, 12-14,16 and 29 are rejected under35 U.S.C. 103(a) as being unpatentable over Jonas et al. US 3,853,878, in view of Mokrosz et al., Med. Chem. Res. 3: 240-248,1993.

Jonas et al. teaches several heaxahydropyrazino[1,2-a]indole compounds, which include those claimed herein. See compound of formula II on col. 1, line50 and note the definition of R. See col. 2 for compounds made, See example 2. Hence it is held that in order to make compounds shown in example 2, Jonas et al. had inherently made the intermediates, which are claimed herein. Note In re Petering et al 133 USPQ 275; In Re Schaumann, 195 USPQ 5.

Instant claims, which were originally compound claims, now recite pharmaceutical composition containing compound of formula I.

The secondary reference, Mokrosz et al., as noted in the above 103 rejection, teaches heaxahydropyrazino[1,2-a]indole and N-ethyl- heaxahydropyrazino[1,2-a]indole as bioactive compounds useful for 5HT receptor. The combined art teaches equivalency of the intermediate compounds with bioactive compounds and hence its pharmaceutical composition.

Thus one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and make compounds variously substituted in heaxahydropyrazino[1,2-a]indole as permitted by the reference and expect resulting compounds (instant compounds) and its pharmaceutical composition to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1-8, 9-18, and 29 are rejected under35 U.S.C. 103(a) as being unpatentable over Bos CA 2,097, in view of Mokrosz et al., Med. Chem. Res. 3: 240-248,1993.

Bos teaches several tetrahydropyrazinoindole compounds, composition and method of use treating several central nervous disorders including obesity. See compound of formula I on page 1 and note the definition of R^1, R^2, and R^3 groups and the diseases for which these compounds are useful. See pages 2-13 for details of the preferred embodiments, schemes for making and pages 13-16 for testing. . See examples 1-14 on page 16-37 and example A, B for composition.

Instant claims differ from Bos in requiring pharmaceutical composition containing compound of formula I, which are hexahydropyrazinoindole

The secondary reference, Mokrosz et al., as noted in the above 103 rejection, teaches heaxahydropyrazino[1,2-a]indole and N-ethyl- heaxahydropyrazino[1,2-a]indole as bioactive compounds useful for 5HT receptor. On page 241, Mokrosz et al. teaches reduction of tetrahydropyrazinoindole to hexahydropyrazinoindole. Mokrosz et al. also demonstrates that both tetrahydropyrazinoindole and hexahydropyrazinoindole are

active in the 5HT assay. See page 243, Table 2. Thus there is a clear-cut teaching of equivalency of both tetrahydropyrazinoindole to hexahydropyrazinoindole in their activity toward 5HT.

Thus one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and make compounds variously substituted in heaxahydropyrazino[1,2-a]indole based on the reduction of tetrahydropyrazino[1,2-a]indole as permitted by the combined references and expect resulting compounds (instant compounds) and its pharmaceutical composition to possess the uses taught by the art in view of the equivalency teaching outline above.

Allowable Subject Matter

Claim 34 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Said claim would be allowed since specific process embraced in this claim is not taught or suggested by the art of record or from a search in the relevant art area.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

8/27/2003